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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/368,630	08/05/99	CENTER	D 12875

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EXAMINER	
BUNNER, B	
ART UNIT	**PAPER NUMBER**
1647	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/368,630	Applicant(s) CENTER ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *34, 36-39, and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33, 35, and 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-42* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647, Examiner Bridget E. Bunner.

Status of Application, Amendments and/or Claims

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 8, 23 March 2000) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (Paper No. 4, 02 November 1999; Paper No. 6, 23 February 2000) are withdrawn.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-33, 35, and 40-41, drawn to an IL-16 antagonist peptide, nucleic acid molecule, and pharmaceutical composition in Paper No. 13 (15 May 2001) and Paper No. 15 (28 June 2001) is acknowledged. The traversal is on the ground(s) that the peptides and nucleic acid molecules of Group I are related to the antibodies of Group II. Applicant indicates that the antibodies are specific for the peptides of Group I and can be prepared once the polypeptide sequence or nucleotide sequence for the polypeptide is provided. Applicant also argues that Groups I, II, and III are merely different aspects of a single invention wherein the methods of Group III use the peptides of Group I and the antibodies of Group II can detect or purify the peptides of Group I. Applicant asserts that restriction requirements are prohibitive in that the requirements impose a financial burden upon the Applicant and contravene the purpose to promote and encourage the progress of science. It is noted that Applicant cites case law to support these assertions. This is not found persuasive because the inventions of Groups I, II, and III are distinct, each from one another. For example,

the protein of Group I can be used in materially different methods other than to make the antibody of Group II, such as in therapeutic or diagnostic methods (e.g., in screening). Additionally, Inventions I and III are related as product and process of use. The inventions are distinct since in the instant case, the peptides may be used for the production of antibodies or in diagnostic assays. Furthermore, the inventions of Groups I, II, and III require a divergent literature search, with no reason to believe that the searches would be co-extensive.

The requirement is still deemed proper and is therefore made FINAL.

The species election requirement at pg 2 of the previous Office Action (12 March 2001) is *withdrawn*. The first elected species of the amino acid sequence of SEQ ID NO: 2 is found to be free of the art.

Claims 34, 36-39, and 42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13 (16 May 2001) and Paper No. 15 (28 June 2001).

Claims 1-33, 35, and 40-41 are under consideration in the instant application.

Information Disclosure Statement

The information disclosure statement filed 17 April 2001 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

1. The disclosure is objected to because of the following informalities:

2. The abstract of the disclosure is objected to because at line 7, the word "acid" is missing the letter "s". Correction is required. See MPEP § 608.01(b).

3. The Brief Description of Drawings at pg 9 for Figure 6 refers to two different blots probed with different antibodies ("upper panel" and "lower panel"). However, Figure 6 only displays one blot.

4. The specification at pg 12, lines 12-13 contains a blank U.S. Application No., which is not clear, concise, and exact.

5. The use of the trademark FICOLL-PAQUE has been noted in this application (see pg 30, line 17). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "IL-16 ANTAGONIST PEPTIDES AND DNA ENCODING THE PEPTIDE".

Appropriate correction is required.

Claim Objections

7. Claims are objected to because of the following informalities:

7a. Claims 6-7, 9, 14-15, 17, 19, 22-23, 25, 27, 33, and 35 recite a "." after the term "X_{aa2}". The "." should be removed.

7b. The word "peptide" in claim 33 should be made plural.

7c. The word "Ileu" in line 2 of claim 27 should be "Ile".

Appropriate correction is required.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-33, 35, and 40-41 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims read on a product of nature in that the claimed polypeptide is not "isolated". Amending the claims to read "isolated" would be remedial.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-33, 35, and 40-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NOs: 2, 5, 6, 17, and 24 and a composition comprising an isolated IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NOs: 2, 5, 6, 17, and 24 and a pharmaceutically acceptable carrier, does not reasonably provide enablement for an IL-16 antagonist peptide, an IL-16 antagonist, an IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32, and 34-38, and a

composition comprising an IL-16 antagonist and a pharmaceutically acceptable carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-33, 35, and 40-41 are directed to an IL-16 antagonist peptide, an isolated nucleic acid molecule coding for an IL-16 antagonist peptide, an IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NOs: 2-7, 9-11, 13-32, and 34-38, and a composition comprising the IL-16 antagonist peptide and a pharmaceutically acceptable carrier. Additionally, the claims recite an IL-16 antagonist and a composition comprising an IL-16 antagonist and a pharmaceutically acceptable carrier. The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of the enabling disclosure for the following reasons.

The specification teaches that the "IL-16 antagonist peptides of the present invention are at least 4 amino acids in length and substantially correspond to the C-terminal sequence of human or murine IL-16 surrounding the Arg/Lys-Arg motif". Preferred IL-16 antagonist peptides of the present invention have the tetrameric peptide $X_{aa0}RX_{aa1}X_{aa2}$, $X_{aa1}X_{aa2}X_{aa0}R$, and $X_{aa1}X_{aa0}RX_{aa2}$ (pg 3-5). The specification also teaches working examples to demonstrate that the isolated antagonist peptides of SEQ ID NOs: 2, 5, 6, 17, and 24 inhibit IL-16 stimulated human T lymphocyte cell migration (pg 34-35). However, the specification does not teach any methods or working examples to demonstrate that the isolated peptides of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32, and 34-38 are capable of inhibiting IL-16 mediated T lymphocyte migration. The specification does not teach that the isolated peptides of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32, and 34-38 retain the functional or structural characteristics of the isolated antagonist

peptides of SEQ ID NOs: 2, 5, 6, 17, and 24. The assumption that the peptides of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32, and 34-38 have biological activities similar to the antagonist peptides of SEQ ID NOs: 2, 5, 6, 17, and 24 cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Kopchick et al. (U.S. patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48). Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites.

Due to the large quantity of experimentation necessary to screen the numerous peptide sequences recited in the claims for antagonistic activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of mutation on protein structure and function (see discussion and recited reference), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

10. Claims 35 and 41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 35 and 41 are directed to a pharmaceutical composition comprising an IL-16 antagonist peptide and a pharmaceutically acceptable carrier.

The specification teaches a composition comprising an isolated IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NOs: 2-7, 9-11, 13-32, and 34-38. The specification does not teach how to use an IL-16 "pharmaceutical" composition without undue experimentation for the treatment of a disease in an animal. The specification lists disorders to be treated (pg 25, lines 5-6; pg 26; lines 27-29; pg 27, lines 1-5), but there are no working examples directed to a particular disorder in an animal or administration of the IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NO: 2-7, 9-11, 13-32, and 34-38 to an animal for treatment. (Note, this issue could be overcome by deleting the word "pharmaceutical" from the claims.)

Due to the large quantity of experimentation necessary to determine the quantity of IL-16 antagonist peptide to be administered, the most effective administration route, and the duration of the treatment, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of the IL-16 antagonist peptide *in vivo,* undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-33, 35, and 40-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Regarding claims 1-33, 35, and 40-41, the acronym and abbreviations "IL-16, Arg, Lys, Thr, Ala, Ser, Ile, Val, Leu" render the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

13. Claims 2-33, and 35 are rejected as being indefinite because it is not clear what type of sequence the claims are referring to. Is it an amino acid sequence or a nucleic acid sequence? (For example, amending the claims to recite "...peptide consisting/comprising an amino acid sequence..." would be remedial.)

14. Claims 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it is unclear whether open or closed term language is intended. See MPEP § 2111.03.

15. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd.

App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1-33 and 35 recite the broad recitations such as $X_{aa0}RX_{aa1}X_{aa2}$ and RRKS, and the claims also recite in parentheses respective SEQ ID NOs, which is the narrower statement of the range/limitation. Amending the claims to specify for example, that $X_{aa0}RX_{aa1}X_{aa2}$ has an amino acid sequence consisting of SEQ ID NO: 1 and RRKS has an amino acid sequence consisting of SEQ ID NO: 2 would be remedial.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

16. Claims 1, 33, 35, and 40-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Center et al. (U.S. patent 6,159, 463). Center et al. teaches isolated amino acid sequences that exhibit lymphocyte chemoattractant factor (LCF) antagonist activity. Center et al. also teaches a composition comprising amino acid sequences that exhibit LCF antagonist activity (col 7-8, 12-15).

Pertinant Prior Art Made of Record

IUIS/WHO Standing Committee on Interleukin Designation. Eur. J. Immunol. 26: 1196, 1996. This reference teaches that IL-16 was originally known as lymphocyte chemoattractant factor (LCF).

Conclusion

No claims are allowable.

It is noted that claim 33 is directed to an isolated nucleic acid molecule encoding any one numerous antagonist peptides. Claim 33 is interpreted to be limited to the nucleic acid molecule that encodes one of the claimed peptides of SEQ ID NOs: 2-7, 9-11, 13-32, and 34-38.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Center et al. J Immunol 128: 2563-2568, 1982.
Cruikshank et al. Proc Natl Acad Sci USA 91: 5109-5113, 1994.
Cruikshank et al. J Immunol 146: 2928-2934, 1991.
Cruikshank et al. Nature 382(6591): 501-502, 1996.
Nicoll et al. J Immunol 163: 1827-1832, 1999.
Liu et al. J Biol Chem 274(33): 23387-23395, 1999.
de Bie et al. Eur J Pharmacol 383: 189-196, 1999.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
August 9, 2001

ELIZABETH KEMMERER
PRIMARY EXAMINER